

REMARKS

Claims 11-14, 16, 20-27, 32-34, 36, 37, 44 and 50-66 are pending and under examination.

Rejection Under 35 U.S.C. § 102

The rejection of claims 11, 13, 14, 16, 21, 22, 24-27, 32, 34, 36, 37, 44 and 50-61 under 35 U.S.C. § 102(b) as allegedly anticipated by Turner et al., Breast Cancer Res. Treatment 46:69 abstract 276 (1997), is respectfully traversed. Applicants respectfully submit that the claimed methods are novel over Turner et al.

The claimed methods are directed to methods related to stage I or stage II breast cancer. Independent claim 16 is directed to a method for prognosis of disease free or overall survival of an individual having a breast cancer tumor by determining, using a BAG 1 specific antibody, the level of BAG 1 protein expression in a sample of the tumor or tumor cells from a body fluid during stage I or stage II of the cancer, wherein a high level of BAG 1 expression relative to a reference level of BAG-1 expression correlates positively with disease free or overall survival. Independent claim 25 is directed to a method for predicting the risk of tumor recurrence or spread in an individual having a breast cancer tumor by determining, using a BAG 1 specific antibody, the level of BAG 1 protein expression in a sample of the tumor or breast tumor cells from a body fluid from the individual during stage I or stage II of said cancer, wherein a high level of BAG 1 expression relative to a reference level of BAG-1 expression correlates negatively with tumor recurrence or spread. Independent claim 27 is directed to a method for screening a breast cancer patient to determine the risk of tumor metastasis or chance of survival by (a) determining, using a BAG 1 specific antibody, the level of expression of BAG 1 protein in a cancerous tissue sample or tumor cells from a body fluid sample from the patient during stage I or stage II of the cancer; and (b) classifying a patient having high levels of expression of BAG 1 protein, relative to a reference level, as being less likely to suffer tumor metastasis or having an increased chance of survival.

Independent claim 34 is directed to a method for determining the proper course of treatment for a patient suffering from breast cancer by (a) determining, using a BAG 1 specific antibody, the level of BAG-1 protein expression in a cancerous tissue sample or tumor cells from

a body fluid from the patient during stage I or stage II of the cancer; (b) identifying a first group of patients having low levels of BAG-1 expression relative to a reference level of BAG-1 expression, which first group of patients may require treatment proper for patients having a lesser chance of survival or being more likely to suffer tumor recurrence or spread; and (c) identifying a second group of patients having high levels of BAG-1 expression relative to a reference level of BAG-1 expression, which second group of patients may require treatment proper for patients having a greater chance of survival and being less likely to suffer tumor recurrence or spread. Independent claim 44 is directed to a method for determining risk of tumor recurrence or spread in a patient suffering from breast cancer by (a) determining, using a BAG 1 specific antibody, the level of expression of BAG-1 protein in a cancerous tissue of a patient during stage I or stage II of the cancer; and (b) classifying the patient as belonging either to a first group of patients having high levels of expression of BAG-1 relative to a reference level of BAG-1 expression, or a second group of patients having low levels of expression of BAG-1 relative to a reference level of BAG-1 expression, wherein the first group has a lower likelihood of tumor recurrence or spread than the second group, thereby determining a lower risk of tumor recurrence or spread in the first group of patients suffering from breast cancer.

Turner et al. describes the characterization of the subcellular location of BAG-1 protein in human breast cancer. BAG-1 expression was determined in 87 breast cancer cases containing invasive carcinoma (IC)(82 cases) or pure ductal carcinoma *in situ* (DCIS)(5 cases), with 53 of the cases having some benign breast epithelium (BBE). Applicants respectfully point out that, in contrast to the assertion in the Office Action on page 5, “BBE patients” are not separate patients to which cancer patients are compared. The 10-year overall survival (OS) and distant disease free survival (DDFS) for breast cancer patients with overexpression of BAG-1 in the nuclear component of BBE was 77% and 81%, respectively, compared to 54% and 40% for BBE with low levels of BAG-1. The 10-year OS and DDFS for patients with overexpression of cytoplasmic BAG-1 in IC specimens was 75% and 70%, respectively, compared to 62% and 35% for tumors with low cytoplasmic BAG-1 levels. It was found that 93% of specimens containing IC had overexpression of BAG-1. Of the 5 cases of pure DCIS, overexpression of BAG-1 was found in 80% of the specimens (40% having nuclear and cytoplasmic and 40% having nuclear only). Of the 53 cases having areas of BBE, overexpression of BAG-1 was found in 47% of specimens. The Turner et al. reference concludes “that the subcellular location of

BAG-1 may have prognostic importance with respect to survival of breast cancer patients” (emphasis added). Thus, Turner et al. provides no teaching of methods for prognosis of breast cancer, predicting the risk of tumor recurrence or spread in an individual having a breast cancer tumor, screening a breast cancer patient to determine the risk of tumor metastasis or chance of survival, or determining the proper course of treatment for a patient suffering from breast cancer in a patient during stage I or stage II of breast cancer, as claimed. At best, Turner et al. suggests that the subcellular location of BAG-1 may have prognostic importance but provides no teaching that the level of BAG-1 protein expression in a sample is prognostic for stage I or stage II of breast cancer.

Turner et al. describes a higher percentage of overexpression of BAG-1 in cancerous IC (93%) and in DCIS (80%) than in benign BBE (47%). Therefore, based on the description in Turner et al., as a tissue becomes cancerous or becomes a more aggressive form of cancer, overexpression of BAG-1 increases. Furthermore, Turner et al. indicates that, in BBE, overexpression of BAG-1 was found to be in a higher proportion in the nucleus alone (30%) than in the cytoplasm and nucleus (13%) or cytoplasm alone (4%). In IC, overexpression of BAG-1 was found to in a higher proportion in the cytoplasm alone (89%) than in the cytoplasm and nucleus (22%) or nucleus alone (4%). From these observations, Turner et al. concludes that the subcellular location of BAG-1 overexpression may be prognostic but provides no teaching that overexpression of BAG-1 would be prognostic for stage I or stage II breast cancer. Absent such a teaching, Applicants respectfully submit that Turner et al. cannot anticipate the claimed methods.

Applicants respectfully submit that the claimed methods are novel over Turner et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

The rejection of claims 11-14, 16, 21, 22, 24-27, 32-34, 36, 37, 44 and 50-61 under 35 U.S.C. § 103 as allegedly obvious over Turner et al., *supra*, in view of Sano et al., U.S. Patent No. 5,665,539, is respectfully traversed. Applicants respectfully submit that the claimed methods are unobvious over Turner et al., alone or in combination with Sano et al.

As discussed above, Applicants respectfully submit that Turner et al. does not teach or suggest the claimed methods. Furthermore, Applicants respectfully submit that Sano et al. does not cure the deficiencies of Turner et al. Therefore, Applicants respectfully submit that the claimed methods are unobvious over Turner et al., alone or in combination with Sano et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 11, 13, 14, 16, 20-22, 24-27, 32, 34, 36, 37, 44 and 50-66 under 35 U.S.C. § 103 as allegedly obvious over Turner et al., *supra*, in view of Sauter et al., Br. J. Cancer 76:494-501 (1997), is respectfully traversed. Applicants respectfully submit that the claimed methods are unobvious over Turner et al., alone or in combination with Sauter et al.

As discussed above, Applicants respectfully submit that Turner et al. does not teach or suggest the claimed methods. Furthermore, Applicants respectfully submit that Sauter et al. does not cure the deficiencies of Turner et al. Therefore, Applicants respectfully submit that the claimed methods are unobvious over Turner et al., alone or in combination with Sauter et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 11, 13, 14, 16, 21-27, 32, 34, 36, 37, 44 and 50-61 under 35 U.S.C. § 103 as allegedly obvious over Turner et al., *supra*, alone or in combination with Takayama et al., Cancer Res. 58:3116-3131 (1998), is respectfully traversed. Applicants respectfully submit that the claimed methods are unobvious over Turner et al., alone or in combination with Takayama et al.

As discussed above, Applicants respectfully submit that Turner et al. does not teach or suggest the claimed methods. Furthermore, Applicants respectfully submit that Takayama et al. does not cure the deficiencies of Turner et al. Therefore, Applicants respectfully submit that the claimed methods are unobvious over Turner et al., alone or in combination with Takayama et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In light of the remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

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To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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